

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 17 May 2001 (17.05.01)	
International application No. PCT/IT00/00321	Applicant's or agent's file reference PCT24458
International filing date (day/month/year) 28 July 2000 (28.07.00)	Priority date (day/month/year) 06 August 1999 (06.08.99)
Applicant CATTANEO, Antonino et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

05 March 2001 (05.03.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Pascal Piriou Telephone No.: (41-22) 338.83.38
--	--

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT
PTO/PCT Rec'd 1 1 FEB 2002

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

BANCHETTI, Marina
Ing. Barzanó & Zanardo Roma S.p.A.
Via Piemonte, 26
I-00187 Roma
ITALIE

Date of mailing (day/month/year) 15 February 2001 (15.02.01)		
Applicant's or agent's file reference PCT24458		IMPORTANT NOTICE
International application No. PCT/IT00/00321	International filing date (day/month/year) 28 July 2000 (28.07.00)	
Priority date (day/month/year) 06 August 1999 (06.08.99)		
Applicant S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,FI,
GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,
MW,MX,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 15 February 2001 (15.02.01) under No. WO 01/10203

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



10/049306

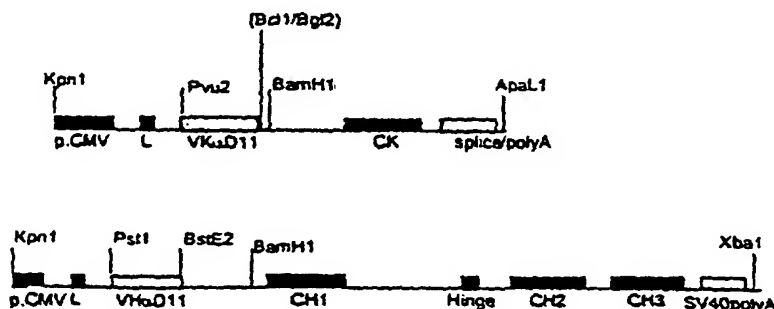
(43) International Publication Date
15 February 2001 (15.02.2001)

PCT

(10) International Publication Number
WO 01/010203 A3

- (51) International Patent Classification⁷: **C12N 15/00**, A01K 67/027, C07K 16/22, C12N 5/10, G01N 33/50, A61P 21/00, 25/00, C07K 16/00
- (74) Agents: **BANCHETTI, Marina et al.**; Ing. Barzanó & Zanardo Roma S.p.A., Via Piemonte, 26, I-00187 Roma (IT).
- (21) International Application Number: PCT/IT00/00321
- (22) International Filing Date: 28 July 2000 (28.07.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
MI99A001783 6 August 1999 (06.08.1999) IT
RM00A000306 5 June 2000 (05.06.2000) IT
- (71) Applicant (for all designated States except US): **S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI** [IT/IT]; Via Beirut, 2-4, I-34014 Trieste (IT).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **CATTANEO, Antonino** [IT/IT]; S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati, Via Beirut, 2-4, I-34014 Trieste (IT). **CAPSONI, Simona** [IT/IT]; S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati, Via Beirut, 2-4, I-34014 Trieste (IT). **RUBERTI, Francesca** [IT/IT]; S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati, Via Beirut, 2-4, I-34014 Trieste (IT).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
12 September 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NON-HUMAN TRANSGENIC ANIMALS FOR THE STUDY OF NEURODEGENERATIVE SYNDROMES



(57) Abstract: Non-human transgenic animals as model study for human pathologies, being transgenic for an antibody are disclosed, in particular non-human transgenic animals for anti-NGF (Nerve Growth Factor) antibody able to mimic different pathologies, as neurodegenerative syndromes, to be used as a model to study said pathologies and provide therapies therefor.

WO 01/010203 A3

RECEIVED
OCT 29 2002
TECH CENTER 1600/2900

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/IT 00/00321

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/00 A01K67/027 C07K16/22 C12N5/10 G01N33/50
 A61P21/00 A61P25/00 C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EP0-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 921 189 A (SANKYO CO ; TOKYO METROPOLITAN INST OF MED (JP)) 9 June 1999 (1999-06-09) the whole document ---	1,2, 17-19, 21,29
X	PICCIOLI P, DI LUZIO A, AMANN R, SCHULIGOI R, SURANI MA, DONNERER J, CATTANEO A.: "Neuroantibodies: ectopic expression of a recombinant anti-substance P antibody in the central nervous system of transgenic mice." NEURON. 1995 AUG;15(2):373-84., XP000102376 cited in the application the whole document --- -/--	1,17-19, 21,24,26

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 September 2001

Date of mailing of the international search report

08. 01. 2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

CHAMBONNET, F

INTERNATIONAL SEARCH REPORT

Int. Patent Application No

PCT/IT 00/00321

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CATTANEO A ; RUBERTI F: "Transgenic mice expressing NGF antibodies during postnatal life." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 22, no. 1-3, 16 November 1996 (1996-11-16), page 753 XP001023821	24,25,31
A	abstract & 26th Annual Meeting of the Society for Neuroscience; Washington, D.C., USA; November 16-21, 1996 ---	1,2,10, 13-19
A	CHEN KAREN S ET AL.: "Disruption of a single allele of the nerve growth factor gene results in atrophy of basal forebrain cholinergic neurons and memory deficits." JOURNAL OF NEUROSCIENCE, vol. 17, no. 19, 1997, pages 7288-7296, XP002177092 abstract ---	3
A	WO 92 08483 A (CHILDRENS MEDICAL CENTER) 29 May 1992 (1992-05-29) the whole document ---	3
P,X	CAPSONI, S. ET AL.: "Alzheimer-like neurodegeneration in aged antinerve growth factor transgenic mice" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA., vol. 97, no. 12, 6 June 2000 (2000-06-06), pages 6826-6831, XP001023701 NATIONAL ACADEMY OF SCIENCE. WASHINGTON., US ISSN: 0027-8424 the whole document ---	1-19, 21-37
P,X	RUBERTI F; CAPSONI S; COMPARINI A; DI DANIEL E; FRANZOT J; GONFLONI S; ROSSI G; BERARDI N; CATTANEO A: "Phenotypic knockout of nerve growth factor in adult transgenic mice reveals severe deficits in basal forebrain cholinergic neurons, cell death in the spleen, and skeletal muscle dystrophy." JOURNAL OF NEUROSCIENCE, vol. 20, no. 7, 1 April 2000 (2000-04-01), pages 2589-2601, XP000102377 cited in the application the whole document ---	1,2,25, 26

	-/--	

INTERNATIONAL SEARCH REPORT

Inte Application No

PC, IT 00/00321

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>CAPSONI S, RUBERTI F, DI DANIEL E, CATTANEO A.: "Muscular dystrophy in adult and aged anti-NGF transgenic mice resembles an inclusion body myopathy." J NEUROSCI RES. 2000 FEB 15;59(4):553-60., XP001023836 the whole document -----</p>	1,2,24, 25

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IT 00/00321

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

As far as claim 23 is directed to a method of treatment of the animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see further information sheet invention 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19 21-34

Non human transgenic animal, being transgenic for an antibody or fragments thereof and having a phenotype reminiscent of a human pathology; cells derivable from said non human transgenic animal and uses thereof; method for the preparation of said animal and uses of said transgenic animal for studying pathology and screening compounds;

2. Claim : 20

A method for an early diagnosis of neurodegenerative diseases comprising the monitoring of the occurrence of the tau hyperphosphorylation and/or amyloid deposition in the back or lower limb skeletal muscle sample of a subject

3. Claim : 35

Use of NGF or derivatives or fragments thereof for the preparation of pharmaceutical compositions able to bind autoanti-NGF antibodies in the brain of AD affected subjects.

4. Claims: 36, 37

Use of NGF or derivatives or fragments thereof for the preparation of pharmaceutical compositions for the treatment of muscular pathologies

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte Application No

PCT/IT 00/00321

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0921189	A	09-06-1999	EP 0921189 A1	09-06-1999
			JP 11220975 A	17-08-1999
			US 6118044 A	12-09-2000

WO 9208483	A	29-05-1992	AU 9059991 A	11-06-1992
			WO 9208483 A1	29-05-1992

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) PCT24458

Box No. I TITLE OF INVENTION: NON-HUMAN TRANSGENIC ANIMALS FOR THE STUDY OF NEURODEGENERATIVE SYNDROMES.

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.
The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati
Via Beirut n. 2-4
34014 TRIESTE - ITALY

☐ This person is also inventor

Telephone No.
040/37871

Facsimile No.
040/3787249

Teleprinter No.

State (that is, country) of nationality:
ITALY

State (that is, country) of residence:
ITALY

This person is applicant ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.
The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CATTANEO Antonino
S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati
Via Beirut n. 2-4
34014 TRIESTE - ITALY

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
ITALY

State (that is, country) of residence:
ITALY

This person is applicant ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

BANCHETTI Marina - CAPASSO Olga - de SIMONE Domenico - FIORUZZI Maria Augusta - IANNONE Carlo Luigi - TALIERCIO Antonio - ZANARDO Giovanni - ING. BARZANO' & ZANARDO ROMA S.p.A. - Via Piemonte 26 - 00187 ROMA - ITALY

Telephone No.
06/4743241

Facsimile No.
06/4870273

Teleprinter No.
625579

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CAPSONI Simona
S.I.S.S.A. Scuola Internazionale Superiore di Studi
Avanzati
Via Beirut n. 2-4
34014 TRIESTE - ITALY

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
ITALY

State (that is, country) of residence:
ITALY

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

PUBERTI Francesca
S.I.S.S.A. Scuola Internazionale Superiore di Studi
Avanzati
Via Beirut n. 2-4
34014 TRIESTE - ITALY

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

<input checked="" type="checkbox"/>	X	AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, UG Uganda, TZ Tanzania, ZW Zimbabwe, MZ Mozambique and any other State which is a Contracting State of the Harare Protocol and of the PCT	
-------------------------------------	---	----	--	--

<input checked="" type="checkbox"/>	X	EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT	
-------------------------------------	---	----	--	--

<input checked="" type="checkbox"/>	X	EP	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT	
-------------------------------------	---	----	---	--

<input checked="" type="checkbox"/>	X	OA	OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)	
-------------------------------------	---	----	--	--

National Patent (if other kind of protection or treatment desired, specify on dotted line):

<input checked="" type="checkbox"/>	X	AE	United Arab Emirates	<input checked="" type="checkbox"/>	X	LC	Saint Lucia
<input checked="" type="checkbox"/>	X	AG	Antigua and Barbuda	<input checked="" type="checkbox"/>	X	LK	Sri Lanka
<input checked="" type="checkbox"/>	X	AL	Albania	<input checked="" type="checkbox"/>	X	LR	Liberia
<input checked="" type="checkbox"/>	X	AM	Armenia	<input checked="" type="checkbox"/>	X	LS	Lesotho
<input checked="" type="checkbox"/>	X	AT	Austria	<input checked="" type="checkbox"/>	X	LT	Lithuania
<input checked="" type="checkbox"/>	X	AU	Australia	<input checked="" type="checkbox"/>	X	LU	Luxembourg
<input checked="" type="checkbox"/>	X	AZ	Azerbaijan	<input checked="" type="checkbox"/>	X	LV	Latvia
<input checked="" type="checkbox"/>	X	BA	Bosnia and Herzegovina	<input checked="" type="checkbox"/>	X	MA	Morocco
<input checked="" type="checkbox"/>	X	BB	Barbados	<input checked="" type="checkbox"/>	X	MD	Republic of Moldova
<input checked="" type="checkbox"/>	X	BG	Bulgaria	<input checked="" type="checkbox"/>	X	MG	Madagascar
<input checked="" type="checkbox"/>	X	BR	Brazil	<input checked="" type="checkbox"/>	X	MK	The former Yugoslav Republic of Macedonia
<input checked="" type="checkbox"/>	X	BY	Belarus	<input checked="" type="checkbox"/>	X	MN	Mongolia
<input checked="" type="checkbox"/>	X	BZ	Belize	<input checked="" type="checkbox"/>	X	MW	Malawi
<input checked="" type="checkbox"/>	X	CA	Canada	<input checked="" type="checkbox"/>	X	MX	Mexico
<input checked="" type="checkbox"/>	X	CH and LI	Switzerland and Liechtenstein	<input checked="" type="checkbox"/>	X	MZ	Mozambique
<input checked="" type="checkbox"/>	X	CN	China	<input checked="" type="checkbox"/>	X	NO	Norway
<input checked="" type="checkbox"/>	X	CU	Cuba	<input checked="" type="checkbox"/>	X	NZ	New Zealand
<input checked="" type="checkbox"/>	X	CZ	Czech Republic	<input checked="" type="checkbox"/>	X	PL	Poland
<input checked="" type="checkbox"/>	X	DE	Germany	<input checked="" type="checkbox"/>	X	PT	Portugal
<input checked="" type="checkbox"/>	X	DK	Denmark	<input checked="" type="checkbox"/>	X	RO	Romania
<input checked="" type="checkbox"/>	X	DM	Dominica	<input checked="" type="checkbox"/>	X	RU	Russian Federation
<input checked="" type="checkbox"/>	X	DZ	Algeria	<input checked="" type="checkbox"/>	X	SD	Sudan
<input checked="" type="checkbox"/>	X	EE	Estonia	<input checked="" type="checkbox"/>	X	SE	Sweden
<input checked="" type="checkbox"/>	X	ES	Spain	<input checked="" type="checkbox"/>	X	SG	Singapore
<input checked="" type="checkbox"/>	X	FI	Finland	<input checked="" type="checkbox"/>	X	SI	Slovenia
<input checked="" type="checkbox"/>	X	GB	United Kingdom	<input checked="" type="checkbox"/>	X	SK	Slovakia
<input checked="" type="checkbox"/>	X	GD	Grenada	<input checked="" type="checkbox"/>	X	SL	Sierra Leone
<input checked="" type="checkbox"/>	X	GE	Georgia	<input checked="" type="checkbox"/>	X	TJ	Tajikistan
<input checked="" type="checkbox"/>	X	GH	Ghana	<input checked="" type="checkbox"/>	X	TM	Turkmenistan
<input checked="" type="checkbox"/>	X	GM	Gambia	<input checked="" type="checkbox"/>	X	TR	Turkey
<input checked="" type="checkbox"/>	X	HR	Croatia	<input checked="" type="checkbox"/>	X	TT	Trinidad and Tobago
<input checked="" type="checkbox"/>	X	HU	Hungary	<input checked="" type="checkbox"/>	X	TZ	Tanzania
<input checked="" type="checkbox"/>	X	ID	Indonesia	<input checked="" type="checkbox"/>	X	UA	Ukraine
<input checked="" type="checkbox"/>	X	IL	Israel	<input checked="" type="checkbox"/>	X	UG	Uganda
<input checked="" type="checkbox"/>	X	IN	India	<input checked="" type="checkbox"/>	X	US	United States of America
<input checked="" type="checkbox"/>	X	IS	Iceland	<input checked="" type="checkbox"/>	X	UZ	Uzbekistan
<input checked="" type="checkbox"/>	X	JP	Japan	<input checked="" type="checkbox"/>	X	VN	Vietnam
<input checked="" type="checkbox"/>	X	KE	Kenya	<input checked="" type="checkbox"/>	X	YU	Yugoslavia
<input checked="" type="checkbox"/>	X	KG	Kyrgyzstan	<input checked="" type="checkbox"/>	X	ZA	South Africa
<input checked="" type="checkbox"/>	X	KP	Democratic People's Republic of Korea	<input checked="" type="checkbox"/>	X	ZW	Zimbabwe
<input checked="" type="checkbox"/>	X	KR	Republic of Korea				Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:
<input checked="" type="checkbox"/>	X	KZ	Kazakhstan				

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM
☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) 06/08/1999 06 AUGUST 1999	MI99A001783	ITALY		
item (2) 05/06/2000 05 JUNE 2000	RM2000A000306	ITALY		
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1) and (2)

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):
ISA /

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (Day/month/year) Number Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 4

description (excluding
sequence listing part) : 51

claims : 4

abstract : 1

drawings : 38

sequence listing part
of description : _____

Total number of sheets : 98

This international application is accompanied by the item(s) marked below:

- ☒ fee calculation sheet
- ☒ separate signed power of attorney
- ☐ copy of general power of attorney; reference number, if any:
- ☐ statement explaining lack of signature
- ☐ priority document(s) identified in Box No. VI as item(s):
- ☐ translation of international application into (language):
- ☐ separate indications concerning deposited microorganism or other biological material
- ☐ nucleotide and/or amino acid sequence listing in computer readable form
- ☐ other (specify):

Figure of the drawings which
should accompany the abstract:

Language of filing of the
international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

CAPASSO Olga

For receiving Office use only

1. Date of actual receipt of the purported international application	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	
6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only

Date of receipt of the record copy
by the International Bureau:

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's
file reference PCT24458

Applicant S.I.S.S.A. Scuola Internazionale Superiore di Studi Avanzati

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE

60.000 T

2. SEARCH FEE

1.829.775 S

International search to be carried out by _____
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 98 sheets.

first 30 sheets

791.934 b1

68

x 17.426

=

1.184.968 b2

remaining sheets

additional amount

Add amounts entered at b1 and b2 and enter total at B

1.976.902 B

Designation Fees

The international application contains _____ designations.

x

=

1.363.136 D

number of designation fees payable (maximum 10) amount of designation fee

Add amounts entered at B and D and enter total at I

3.340.038 I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT (if applicable)

P

5. TOTAL FEES PAYABLE

5.229.813

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐

authorization to charge
deposit account (see below)

☒

bank draft

☐

coupons

☐

cheque

☐

cash

☐

other (specify):

☐

postal money order

☐

revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION (this mode of payment may not be available at all receiving Offices)

The RO/ _____ ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐

is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐

is hereby authorized to charge the fees for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

Deposit Account No.

Date (day/month/year)

Signature

PCT COOPERATION TREATY

JC

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

BANCHETTI, Marina
Ing. Barzanò & Zanardo Roma S.p.A.
Via Piemonte, 26
I-00187 Roma
ITALIE

Date of mailing (day/month/year) 14 December 2000 (14.12.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference PCT24458	
International application No. PCT/IT00/00321	International filing date (day/month/year) 28 July 2000 (28.07.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 06 August 1999 (06.08.99)
Applicant S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
06 Augu 1999 (06.08.99)	MI99A001783	IT	28 Nove 2000 (28.11.00)
05 June 2000 (05.06.00)	RM00A000306	IT	28 Nove 2000 (28.11.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Eugénia Santos

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY


PCT

From the INTERNATIONAL BUREAU

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:


 BANCHETTI, Marina
 Ing. Barzanó & Zanardo Roma S.p.A.
 Via Piemonte, 26
 I-00187 Roma
 ITALIE

Date of mailing (day/month/year) 17 May 2001 (17.05.01)		
Applicant's or agent's file reference PCT24458		IMPORTANT INFORMATION
International application No. PCT/IT00/00321	International filing date (day/month/year) 28 July 2000 (28.07.00)	
Priority date (day/month/year) 06 August 1999 (06.08.99)		
Applicant S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI et al		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

National : AU, BG, CA, CN, CZ, DE, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

National : AE, AG, AL, AM, AT, AZ, BA, BB, BR, BY, BZ, CH, CU, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, MZ, PT, SD, SG, SI, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:

Pascal Piriou

Telephone No. (41-22) 338.83.38

PCT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

CAPASSO, Olga
BARZANO & ZANARDO ROMA S.P.A.
26, Via Piemonte
00187 ROMA
ITALIE

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing
(day/month/year)

26.03.01

Applicant's or agent's file reference
PCT24458

IMPORTANT NOTIFICATION

International application No.
PCT/IT 00/00321

International filing date (day/month/year)
28/07/2000

Priority date (day/month/year)
06/08/1999

Applicant

S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI ...

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

05/03/2001

2. This date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. (+49-89) 2399-0, Tx: 523656 epmu d
Fax: (+49-89) 2399-4465

Authorized officer

CHURCHER G

Tel. (+49-89) 2399-2545



Sig. UC

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT Rec'd 05 JUN 2002

To:

CAPASSO, Olga
BARZANO & ZANARDO ROMA S.P.A.
26, Via Piemonte
00187 ROMA
ITALIE

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing

(day/month/year)

08.04.2002

Applicant's or agent's file reference

PCT24458

IMPORTANT NOTIFICATION

International application No.

PCT/IT00/00321

International filing date (day/month/year)

28/07/2000

Priority date (day/month/year)

06/08/1999

Applicant

S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI ...

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Hingel, W


Tel. +49 89 2399-8717



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT24458	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IT00/00321	International filing date (day/month/year) 28/07/2000	Priority date (day/month/year) 06/08/1999
International Patent Classification (IPC) or national classification and IPC A01K67/00		
Applicant S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI ...		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Basis of the reportII <input type="checkbox"/> PriorityIII <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input type="checkbox"/> Certain observations on the international application		
Date of submission of the demand 05/03/2001	Date of completion of this report 08.04.2002	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Huber, A Telephone No. +49 89 2399 8173	



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IT00/00321

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-51 as originally filed

Claims, No.:

1-37 as originally filed

Drawings, sheets:

1/38-38/38 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IT00/00321

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 23 (IA); 20, 35-37.

because:

☒ the said international application, or the said claims Nos. 23 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 20, 35-37.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 19, 22-23, 26-28, 30-34

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IT00/00321

	No:	Claims	1-18, 21, 24, 25, 29
Inventive step (IS)	Yes:	Claims	22, 23, 26-28, 30-34
	No:	Claims	19
Industrial applicability (IA)	Yes:	Claims	1-19, 21-22, 24-34
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 23 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

For the assessment of Claim 23 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2. The IPEA agrees with the finding of the ISA to lack of unity of invention. Preliminary examination is restricted to those claims for which an international search report has been established.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: EP-A-0 921 189 (SANKYO CO ;TOKYO METROPOLITAN INST OF MED (JP))
9 June 1999 (1999-06-09)

D2: CATTANEO A ; RUBERTI F: 'Transgenic mice expressing NGF antibodies during postnatal life.' SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 22, no. 1-3, 16 November 1996 (1996-11-16), page 753 XP001023821 & 26th

Annual Meeting of the Society for Neuroscience; Washington, D.C., USA;
November 16-21, 1996

2. D1 discloses the preparation of a non-human transgenic animal which is transgenic for an antibody or a fragment thereof. The antibody has an IgE heavy chain constant region which can bind the IgE receptor on mast cells. The transgenic animals are useful as allergy models.

Since allergy falls under the broad term "immune disorder", the subject-matter of Claims 1, 2, 17, 18, 21 and 29 lacks novelty in view of D1 (Art. 33(2) PCT).

3. D2 discloses the preparation of mice which are transgenic for anti-NGF antibodies (aD11). The antibody is expressed in the CNS of adult mice. The mice are said to provide a useful model to study the role of NGF in adult mice.

D2 is novelty-destroying for the subject-matter of Claims 24 and 25. Moreover, the transgenic mice of D2 inherently must exhibit the same phenotypic markers as described in present application because the same antibody (aD11) is expressed. D2 is therefore also novelty-destroying for the subject-matter of Claims 1-18 and 21.

The selection of the mouse strain BS6JL does not involve inventive activity. It has not been shown in the application that the use of this specific strain is associated with a specific technical effect.

4. The claims which are directed to the use of the transgenic animals (or of cells derived therefrom) for the study of neurodegenerative syndromes of e.g Alzheimer's disease or for selecting pharmacologically effective compounds have not been disclosed or rendered obvious in D2.

The subject-matter of Claims 22-23 and 26- 34 is therefore considered as novel and inventive (Art. 33(2) and (3) PCT).

5. The claims shall reflect the actual contribution of an invention to the art. In the present case, applicants have prepared transgenic animals for anti-NGF antibody which can be used as a model to study human neurodegenerative pathologies. Claim 1, however, is directed to a transgenic animal which is transgenic for **any** antibody and having a phenotype reminiscent of a human pathology. The application does not

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IT00/00321

provide support for transgenic animals secreting an antibody other than anti-NGF antibody. The present breadth of Claim 1 is therefore not justified by the limited disclosure of the application.

g.vc

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

BARZANO & ZANARDO ROMA S.P.A.
Attn. CAPASSO, Olga
26, Via Piemonte
00187 ROMA
ITALY

Date of mailing
(day/month/year)

08/01/2002

Applicant's or agent's file reference

PCT24458

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/IT 00/00321

International filing date

(day/month/year)

28/07/2000

Applicant

S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI ...

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Carla Louro

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PCT24458	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/ IT 00/ 00321	International filing date (day/month/year) 28/07/2000	(Earliest) Priority Date (day/month/year) 06/08/1999
Applicant S.I.S.S.A. SCUOLA INTERNAZIONALE SUPERIORE DI ...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

1a

☐ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

As far as claim 23 is directed to a method of treatment of the animal body,
the search has been carried out and based on the alleged effects of the
composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see further information sheet invention 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-19 21-34

Non human transgenic animal, being transgenic for an antibody or fragments thereof and having a phenotype reminiscent of a human pathology; cells derivable from said non human transgenic animal and uses thereof; method for the preparation of said animal and uses of said transgenic animal for studying pathology and screening compounds;

2. Claim : 20

A method for an early diagnosis of neurodegenerative diseases comprising the monitoring of the occurrence of the tau hyperphosphorylation and/or amyloid deposition in the back or lower limb skeletal muscle sample of a subject

3. Claim : 35

Use of NGF or derivatives or fragments thereof for the preparation of pharmaceutical compositions able to bind autoanti-NGF antibodies in the brain of AD affected subjects.

4. Claims: 36, 37

Use of NGF or derivatives or fragments thereof for the preparation of pharmaceutical compositions for the treatment of muscular pathologies

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/00 A01K67/027 C07K16/22 C12N5/10 G01N33/50
 A61P21/00 A61P25/00 C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 921 189 A (SANKYO CO ;TOKYO METROPOLITAN INST OF MED (JP)) 9 June 1999 (1999-06-09) the whole document ---	1,2, 17-19, 21,29
X	PICCIOLI P, DI LUZIO A, AMANN R, SCHULIGOI R, SURANI MA, DONNERER J, CATTANEO A.: "Neuroantibodies: ectopic expression of a recombinant anti-substance P antibody in the central nervous system of transgenic mice." NEURON. 1995 AUG;15(2):373-84., XP000102376 cited in the application the whole document --- -/--	1,17-19, 21,24,26

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 September 2001

Date of mailing of the international search report

08. 01. 2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

CHAMBONNET, F

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CATTANEO A ; RUBERTI F: "Transgenic mice expressing NGF antibodies during postnatal life." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 22, no. 1-3, 16 November 1996 (1996-11-16), page 753 XP001023821	24,25,31
A	abstract & 26th Annual Meeting of the Society for Neuroscience; Washington, D.C., USA; November 16-21, 1996	1,2,10, 13-19
A	--- CHEN KAREN S ET AL.: "Disruption of a single allele of the nerve growth factor gene results in atrophy of basal forebrain cholinergic neurons and memory deficits." JOURNAL OF NEUROSCIENCE, vol. 17, no. 19, 1997, pages 7288-7296, XP002177092 abstract	3
A	--- WO 92 08483 A (CHILDRENS MEDICAL CENTER) 29 May 1992 (1992-05-29) the whole document	3
P,X	--- CAPSONI, S. ET AL.: "Alzheimer-like neurodegeneration in aged antinerve growth factor transgenic mice" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA., vol. 97, no. 12, 6 June 2000 (2000-06-06), pages 6826-6831, XP001023701 NATIONAL ACADEMY OF SCIENCE. WASHINGTON., US ISSN: 0027-8424 the whole document	1-19, 21-37
P,X	--- RUBERTI F; CAPSONI S; COMPARINI A; DI DANIEL E; FRANZOT J; GONFLONI S; ROSSI G; BERARDI N; CATTANEO A: "Phenotypic knockout of nerve growth factor in adult transgenic mice reveals severe deficits in basal forebrain cholinergic neurons, cell death in the spleen, and skeletal muscle dystrophy." JOURNAL OF NEUROSCIENCE; vol. 20, no. 7, 1 April 2000 (2000-04-01), pages 2589-2601, XP000102377 cited in the application the whole document --- -/--	1,2,25, 26

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	CAPSONI S, RUBERTI F, DI DANIEL E, CATTANEO A.: "Muscular dystrophy in adult and aged anti-NGF transgenic mice resembles an inclusion body myopathy." J NEUROSCI RES. 2000 FEB 15;59(4):553-60., XP001023836 the whole document -----	1,2,24, 25

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0921189	A	09-06-1999	EP 0921189 A1	09-06-1999
			JP 11220975 A	17-08-1999
			US 6118044 A	12-09-2000

WO 9208483	A	29-05-1992	AU 9059991 A	11-06-1992
			WO 9208483 A1	29-05-1992
